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EXAMINER	
PALENIK, JEFFREY T	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,126	HISSINK, CATHARINA EVERDINA	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-17,27 and 31-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-17,27 and 31-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's amendments and remarks filed 24 November 2008. The Examiner acknowledges the following:

Claims 2, 18-26 and 28-30 have been cancelled.

Claims 31-37 have been added. Support for the claims is found in Applicant's originally submitted claims 11 and 15-17.

Claims 1, 3, 5, 7-12 and 15-17 have also been amended. Claim 1 incorporates the limitations of cancelled claim 2 as well as the "random" limitation of claim 10. Claim 3 removed the "optionally" limitation. Claims 5, 8 and 9 amended their respective dependencies. Claim 10 removed the "random" limitation and incorporated it into the independent claim. Claims 11 and 15-17 each have the narrower limitations removed and set forth in the aforementioned new claims 31-37. Though it is indicated as having been amended, it is not clear that anything has been amended within claim 12. While no support is provided for the amendments made to the above claims, none are construed as containing new matter since the limitations were part of the original disclosure. Similarly, no support was provided for the editorial amendments to claims 7, 9 and 15. However, a brief search of the disclosure reveals support on pages 12-13.

Thus, claims 1, 3-17, 27 and 31-37 now represent all claims currently under consideration.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statements (IDS) have been submitted for consideration.

WITHDRAWN OBJECTIONS/REJECTIONS

Objection to the Specification

Applicant's amendment to the Abstract of the Invention has been considered fully and is persuasive. Thus, said objection has been **withdrawn**.

Objection to the Claims

Applicants' amendments to both claims 1 and 15, further defining the variables used, have been considered fully and are persuasive. Thus, said objections have been **withdrawn**.

Rejection under 35 USC 112

Applicants' amendments to claims 3, 8, 11 and 15-17, as discussed above, render moot their rejections, under 35 USC 112, second paragraph. Thus, said rejections have been **withdrawn**.

Rejection under 35 USC 102(b)

Applicants' amendments and remarks, particularly those directed to claim 1, render moot the rejection to claims 1, 3-10 and 12-17, under 35 USC 102(b), as being anticipated by the journal article by Penco et al. (*Macromolecular Chemistry and Physics*). The amendment made to claim 1 incorporates the limitation that the segments of the copolymer are "randomly distributed in the copolymer". This limitation is imported from claim 10 where it was previously interpreted as part of a product-by-process limitation. Since it is now interpreted by the Examiner as a structural property of the composition, said rejection now stands **withdrawn**.

Rejection under Nonstatutory Double Patenting

Applicants' submission of a Terminal Disclaimer on behalf of co-pending application 10/586,226, is acknowledged. Said Disclaimer has been approved, thus rendering moot the present rejection on the grounds of provisional nonstatutory obviousness-type double patenting. Thus, said rejection has been **withdrawn**.

MAINTAINED REJECTIONS

The following rejection is maintained from the previous Office Correspondence dated 22 July 2008 since the art which was previously cited continues to read on the amended limitations.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-17 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penco et al (*Macromolecular Chemistry and Physics*) in view of Cohn et al. (US Pre-Grant Publication 2001/0009662).

The instant claims are directed to a biodegradable multiblock copolymer comprising two pre-polymer components (A) and (B), which are linked by a multifunctional chain-extender, as described above. The composition is further limited wherein the aliphatic chain-extender is polyethylene glycol (PEG) having a molecular weight ranging from 150-4000, also as discussed above. Independent claim 27 recites an implant device comprising a copolymer of claim 1.

The teachings of Penco et al. are discussed in the previous Office Correspondence and are reiterated below for Applicant's convenience:

The instant claims are directed to a biodegradable multiblock copolymer comprising two pre-polymer components (A) and (B), which are linked by a multifunctional chain-extender (claims 1, 10 and 12). Pre-polymer (A) has glass transition temperature (T_g) is less than 37°C, and pre-polymer (B) has a melting point temperature (T_m) between 40-100°C. Claims 10 and 12 both further limit claim 1 such that they recite how to obtain pre-polymers (A) and (B), respectively. However, the aforementioned limitations are product-by-process limitations and, per MPEP 2113, hold no patentable weight. The chain-extender is recited as an aliphatic polyether (claims 2 and 9). Pre-polymer (A) is further limited to comprising ester groups such as diols, dicarboxylic acids and hydrocarboxylic acids as well as other cyclic and/or non-cyclic monomers, and/or carbonate groups (claims 3 and 5-8). Claim 4 limits the composition of claim 1 to further comprising a polyether pre-polymer. Pre-polymer (B) is limited to poly-ε-caprolactone (claims 13 and 14), wherein it is further limited by its average molecular weight

(claim 15) and its percent weight representation within the composition (claim 16). Claim 17 recites intrinsic viscosity limitations to the composition of claim 1.

Penco et al. teach multi-block compolymers having the structure of poly(ester-carbonate)s obtained via chain extension involving poly(lactic-glycolic acid) oligomers (PLGA) and oligomeric poly(ε-caprolactone)s or PCDTs (Abstract). Chain extension of the PLGA-PCDT multi-block copolymer compounds is taught through the additional inclusion of poly(ethylene glycol) or PEG oligomers (¶2 Introduction). Tables 1 and 4 both teach molecular characterizations for PLGA-PCDT block copolymers, and more specifically the following compounds: PLGA 50/50-PCDT1250 and PLGA 50/50-PCDT2000, as shown below:

Molecular Characteristics:	*PLGA-PCDT Block Copolymers*	
Table 1 Parameter	*PLGA 50/50-PCDT1250*	*PLGA 50/50-PCDT2000*
Intrinsic Viscosity [η] (dl/g) *Claimed: [η] = at least 0.1 dl/g*	*1.20 dl/g*	*0.82 dl/g*
Table 3 Parameters		
PCDT in wt. % *Claimed: %-wt. = 10-90%*	*39.31 %*	*50.89 %*
Glass Transition Temp. (T_g) *Claimed: (T_g) is <37°C*	*-57.9 °C*	*-45.3 °C*
Melting Point Temp. (T_m) *Claimed: (T_m) is 40-100°C*	*40.3 °C*	*49.4 °C*

The pre-polymer (B), represented by the PCDT component, in both examples is greater than 1000 (e.g. PCDT1250 and PCDT2000).

Penco neither expressly teaches the use of any particular weight of PEG or incorporation of the copolymer composition into a medical delivery device such as an implant.

Cohn et al. teaches a polymeric composition comprising coupled AB diblocks, where A is a polyester unit derived from the polymerization of compounds such as lactic acid, lactide, glycolic acid, glycolide, ε-caprolactone, δ-valerolactone, trimethylene carbonate and p-dioxanone and B is derived from a compound such as a hydroxyl-terminated compound initiating the polymerization of said monomers from said polyester unit (e.g. ε-caprolactone). Said AB diblock being further reacted with one or more coupling or crosslinking agents to form di-diblocks or multi-block polymers (claim 1). Polyethylene glycol, also known as polyethylene oxide (PEO) and polyoxyethylene (POE), is taught as being used to extend the polymer chains of di- and tri-blocks of the invention (see ¶[0092]). Example 3 teaches the synthesis of [MPEG 550-HDI]2-[(I)LA4-PPG1000-LA4], which is an ACA tri-block of lactic acid (LA)-polypropylene glycol 1000 (PPG1000)-LA where the tri-block chain is extended using polyethylene glycol methyl ether having a molecular weight of 550. The product is characterized as having a glass transition temperature around -44°C, having two melting temperatures (e.g. endotherms) at 11°C and 34°C, and a viscosity value of 43,000 centipoise (cps) at 27°C. Pre-polymer (B), which in the case of Example 3 is the PPG1000 component, was added in the amount of 40 grams and represents approximately 24.5% of the entire composition produced by the Example. Example 8 teaches synthesis of another tri-block polymer which uses

poly-caprolactone having a molecular weight of 1250. The polymers of the present invention are also taught as being used in various forms, structures such as films, rods, cylinders, gels and biodegradable articles, among many others, which have medical uses such as preventing tissue-to-tissue or tissue-to-device adhesion (see ¶¶[0093] and [0094]).

Cohn et al. does not expressly teach pre-polymer melting point temperatures ranging as instantly claimed. Intrinsic viscosity is also not taught as being used to characterize any of the practiced multi-block copolymer products.

In view of the combined teachings of the prior art, one of ordinary skill in the pharmaceutical art would have been motivated to react the instantly claimed cyclic and/or non-cyclic monomer precursors in combination with the aliphatic polyether chain extending polymers with a reasonable expectation of successfully achieving the claimed biodegradable multiblock copolymer formulation of the instant invention. Such would have been obvious in the absence of evidence to the contrary since both Penco et al. and Cohn et al. teach overlapping components and variations to their respective compositions, which can be incorporated into the instant composition as well as the instant method for closing wounds and preventing microbial growth. Though the compositions practiced by Penco et al. are not expressly taught as being implemented into an implant device, Penco does provide a broad teaching stating that all the products synthesized show similar or lower degradation rates compared to typical samples of PLGA normally used as components with drug delivery systems (see *Conclusion* "4") thereby providing motivation for an artisan of ordinary skill to implement the practiced invention into

implantable and biodegradable medical devices such as those taught by Cohn et al. (see ¶[0093]). Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

RESPONSE TO ARGUMENTS

Applicant's arguments with regard to the rejection of claims 1, 3-17 and 27 under 35 USC 103(a) over Penco et al. in view of Cohn et al. et al. have been fully considered, but they are not persuasive.

Applicant alleges that neither of the references teaches or suggests: 1.) linking copolymer segments using an aliphatic chain extender, 2.) that the multiblock copolymers are randomly segmented, per the amended claim 1, or 3.) any of the advantages of the composition.

In response, the Examiner respectfully submits that the Abstract of Penco expressly teaches establishing multi-block copolymers via a chain-extension reaction involving poly(lactic-glycolic acid) oligomers (PLGA). One of the well-known properties of PLGA is that it is an aliphatic or linear polymer. Thus, its use as taught by Penco, meets the limitation of linking segments using an aliphatic chain-extender. Penco further teaches on page 1740 (*Molecular Characteristics*), that the PLGA-PCDT block copolymer samples had different compositions of the PLGA blocks as well as different lengths of the PCDT blocks. Thus, since the PLGA oligomers may differ in their composition (e.g. mole ratio of LA/GA), it follows that Penco suggests that different polymers of PLGA can reside within the same PLGA-PCDT copolymer.

Lastly, in response to Applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e.,

"important advantages") are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For these reasons, Applicants' arguments are found unpersuasive. Said rejection is therefore maintained.

NEW REJECTIONS

In light of Applicant's amendments, most notably to claim 1, as well as the newly added claims 31-37, the following rejections have been newly added:

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 4, 9, 13, 14 and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohn et al. (US Pre-Grant Publication 2001/0009662).

The instantly amended claim 1 is drawn to a multiblock copolymer comprising pre-polymer (A) and pre-polymer (B), wherein (A) and (B) are linked by an aliphatic chain extender and wherein the segments are randomly distributed within the copolymer. Amended claim 3 further limits claim 1 such that pre-polymer (A) comprises ester and/or carbonate croups. Claim 31 further limits claim 3, such that the composition further comprises polyethers. Claims 4, 9, 32 and 33 further limit the composition of claim 1 such that it further comprises polyethylene glycol (PEG) having a molecular weight between 300-1,000 (e.g. PEG400). Claims 13 and 14 further limit the pre-polymer (B) of claim 1, to poly-ε-caprolactone. Claims 34 and 35 further limit claim 14 such that pre-polymer (B) has an average molecular weight of greater than 2,000 and 3,000, respectively (e.g. PCL 4,000). Claim 36 recites that pre-polymer (B) is present between 30-50 wt% of the composition. With regard to the intrinsic viscosity limitation recited in claim 37, which states that the composition of claim 1 has "an intrinsic viscosity of between 1-4 dL/g"; until some material difference in the properties of the composition are demonstrated, said limitation is considered by the Examiner to be directed towards the composition, which is instantly claimed.

Cohn et al. expressly teaches the limitations of claims 1, 3, 4, 9 and 31 at ¶¶[0092] and [0012], such that a composition is administered which comprises ACA triblock copolymers which are chain-extended and comprise polyethylene oxide ¶[0092]. Paragraph [0012] further teaches that block "A" of the triblock is a polyester which is preferably derived from the polymerization of monomers such as lactide, glycolide, ε-caprolactone, δ-valerolactone,

trimethylene carbonate, 1,4-dioxane-2-one and p-dioxanone (e.g. cyclic monomers), lactic, glycolic and/or hydroxybutyric acids (e.g. non-cyclic monomers), as well as mixtures thereof. Paragraph [0092] further teaches that block "A" also preferably comprises aliphatic ester units. The teaching of ε-caprolactone, δ-valerolactone and p-dioxanone are expressly taught examples of both pre-polymers (A) and (B) of claims 6-8 and 13-14. Regarding the limitations of the instant claims 32 and 33, the polyether compound polyethylene glycol (PEG) is expressly taught as a preferred embodiment of block "C" of the triblock copolymer and is even more preferably taught as ranging in size from 400 to 10,000 Daltons ¶[0102]. The limitations of pre-polymer (B) set forth in claims 34-36 are taught by Example 10, which teaches the formation of a copolymer composition using a caprolactone polyester compound having a molecular weight of 4,000. Also, in Example 10, it is taught that PCL 4000 represents 20 grams of a 66 gram formulation (e.g. about 30%).

It would have been *prime facie* obvious to a person of ordinary skill in the art at the time the invention was made to have prepared the instantly claimed multiblock copolymer, particularly in view of the teachings of Cohn et al. Given the following notable and aforementioned properties of block "A" of the ACA triblock copolymer:

- that it is a polyester which may be formed from a large selection of different monomer building blocks which read on the compounds of both of the instantly claimed pre-polymers (A) and (B), and that
- it preferably comprises aliphatic chain extensions,

it follows that the ordinarily skilled artisan would have been highly motivated to use routine experimentation to polymerize chemically distinct polyester "A" blocks and link them

aliphatically, in order to produce the instantly claimed multiblock copolymer chain. Furthermore, Examples 8 and 10, respectively teach the use of larger weight polyester compounds, most notably PCL1250 and PCL4000. Therefore, in view of these combined teachings of Cohn, it would also have been within the purview of the skilled artisan to prepare polymerized "A" blocks comprising repetitive monomer units of ε-caprolactone, in order to achieve the instantly claimed, higher molecular weight embodiments of pre-polymer (B).

Cohn et al. do not expressly teach pre-polymer (B) (e.g. polycaprolactone) as being present between 30-50 wt% of the composition, as claimed by Applicant. Since the values of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill, in view of the teachings of Cohn, to prepare a multiblock copolymer composition comprising 30-50 wt% of polycaprolactone, particularly in view of ¶[0135] which teaches that an amount of the "A" blocks may comprise at least about 25-30% by weight of the ACA triblock copolymers. This teaching is interpreted as reading on weight percentages which are greater than 30 wt% and which include 50 wt%, though not expressly so. The teachings of PCL1250 and PCL4000 in Examples 8 and 10 supports the optimization of the weight of PCL and thus its overall compositional weight. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicant's invention.

All claims have been rejected; no claims are allowed.

CONCLUSION

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615